IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND INTERFERENCES

Appellants	:	BARTHOLOMAUS, Johannes
Serial No.	:	10/596,194 (U.S. Patent Application Publication 2007-0071796)
Filing Date	:	2 June 2006
For	:	ADMINISTRATION FORM BASED ON CROSS-LINKED HYDROPHILIC POLYMERS
Examiner	:	YU, Gina C.
Art Unit	:	1617

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APPEAL BRIEF UNDER 37 C.F.R. 41.37

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Commissioner for Patents
P.O. Box 1450
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Sir:

This Appeal Brief is being filed in response to the final rejection mailed on 29 April 2011 and Notice of Appeal filed on 28 October 2011.

The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0320.

(I) REAL PARTY IN INTEREST

The real party in interest in this appeal is the assignee, LTS Lohmann Therapie-Systeme AG, who is the owner of this application by assignment from the inventor (Reel 017714/Frame 0165).

(II) RELATED APPEALS AND INTERFERENCES

Appellant is not aware of any related appeals or interferences which directly affect or are directly affected by or have bearing on the Board's decision in the pending appeal.

(III) STATUS OF CLAIMS

Claims 1-6, 15 and 18-22 are under examination and were finally rejected in the Office Action mailed on 29 April 2011.

(IV) STATUS OF AMENDMENTS

No amendments were filed after the 29 April 2011 Office Action and it is believed that all other amendments have been entered.

(V) SUMMARY OF CLAIMED SUBJECT MATTER

Claim 1 is the only independent claim under appeal and is directed to a dosage form in film form for transmucosal or transdermal administration of at least one active ingredient and/or nutrient to a living creature comprising at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydrophilic polymers which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers characterized in that hydroxypropylmethylcellulose is used as hydrophilic polymer and the hydrophilic polymer has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

Support for this claim can be found throughout the specification, e.g., page 2, lines 4-12, lines 18-21 ("a dosage form in film form for transmucosal or transdermal administration of at least one active ingredient and/or nutrient to a living creature comprising at least one active ingredient-containing and/or nutrient-containing layer"); page 3, lines 8-18 ("30% to 60% by weight of glycerol"), line 25 ("hydroxypropylmethylcellulose"), lines 27-28 ("in-situ") and lines 35-36 ("crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid").

(VI) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Claim 15 was rejected under 35 U.S.C. 112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention when reciting "the transmucosal or transdermal administration is buccal administration".

B. Claims 1, 6-15 and 18-22 were rejected under 35 U.S.C. 103(a) as allegedly being obvious over Rupprecht et al. (U.S. Patent 6,780,504 - "Rupprecht") in view of Becher (U.S. Patent 6,153,222) and Zerbe et al. (U.S. Patent 6,177,096 - "Zerbe").

C. Claims 1, 6-15 and 18-22 were rejected under 35 U.S.C. 103(a) as allegedly being obvious over Rupprecht et al. (U.S. Patent 6,780,504 - "Rupprecht") in view of Becher (U.S. Patent 6,153,222) and Lydzinski et al. (U.S. Patent 6,177,096 - "Lydzinski").

(VII) ARGUMENTS

A. 35 U.S.C. 112, second paragraph rejection (claim 15)

Claim 15 is not indefinite as one of ordinary skill in the art would understand the scope and meaning buccal administration

Claim 1 which encompassed the scope of administration being either transmucosal or transdermal. Claim 15 is dependent upon claim 1 and one of ordinary skill in the art would understand that the scope of administration has been limited to buccal administration. (If it would serve to expedite matters, the applicants authorize an Examiner's amendment to delete the phrase "or transdermal" if this is the only matter precluding allowability).

B. 35 U.S.C. 103(a) rejection (Claims 1, 6-15 and 18-22 - Rupprecht, Becher, Zerbe)

1. Background

As noted in the appellants' earlier response, plasticizers represent an organic compound added to a high polymer both to facilitate processing and to increase the flexibility and toughness of the final product by internal modification (solvation) of the polymer molecule. (see footnote 1 from page 7 of appellants 9 February 2011 response).

The appellants' specification discloses that for better handling of relatively brittle polymer films, i.e. in particular to increase the elasticity, softness and flexibility, plasticizers are employed in an amount of up to 20% by weight based on the amount of polymer.

When the percentage amounts of plasticizer are relatively high, phase separations may occur, e.g. due to crystallization, so that the films are no longer transparent and their physical properties such as the tear strength are adversely affected. For example, addition of 30% by weight of triethyl citrate, based on the total amount of a crosslinked hydrophilic polymer, leads to white films. The plasticizer may in fact separate out of the film. (See page 2, lines 23-37 of the appellants' specification).

2. Combination of Rupprecht, Becher and Zerbe does not teach the use of 30% to 60% by weight of glycerol as a plasticizer in the appellants' dosage form

Rupprecht refers to a multi-layer film which includes an active substance containing layer which may be produced from a suitable film-forming, water soluble polymer (including hydroxypropylmethylcellulose) and a crosslinking agent (including tannins). See col. 3, lines 1-3 and lines 15-17.

However, the final rejection acknowledges that both Rupprecht and Becher do not teach adding glycerol in an amount of 30% to 60% by weight (see page 4, lines 13-14 and lines 21-22).

The entire specification of Rupprecht does not mention the use of a plasticizer or glycerol as part of their multi-layer film.

Becher does mention the use of a softener which includes polyethylene glycol and glycerol, but not the specific amount and not in the context of a film such as Rupprecht's. Becher refers to a volume-expandable, sheet-like application form which has a highly absorbent hydrogel former which swells on contact with water and assumes several times its original volume (see Abstract of Becher).

Unsurprisingly, because Becher is referring to a highly absorbent hydrogel former, Becher does not use a hydroxypropylmethylcellulose crosslinked with tannins and/or partially neutralized polyacrylic acid.

Becher refers to the use of crosslinked polymers like carboxyvinyl copolymers (e.g. AquaKeep®) and/or crosslinked polyvinyl pyrrolidone (e.g. Kollidone® 90) as film formers in combination with glycerol as softener carboxyvinyl copolymers is a super absorbent polymer based on polyacrylate. Polyvinylpyrrolidone (PVP) is a water-soluble polymer made from the monomer N-vinylpyrrolidone (col. 2, lines 34-39, 56-63).

Zerbe is relied upon for a teaching for the specific amount of glycerol especially with respect to Example 1 (6 g of glycerol and 30 g of hydroxypropylmethyl cellulose was used - 20% by weight which is still outside the appellants' claimed range of 30% to 60% by weight).

However, Zerbe refers to film forming ***non-crosslinked*** polymers comprising preferred water-soluble polymers selected from water-soluble cellulose derivates and polyacrylates, among others and one or more plasticizers or surfactants and one or more polyalcohols (col. 2, line 32-36). Glycerol is mentioned as an example of a polyalcohol (col. 3, line 10-15). The references teach 20% of glycerol based on the total amount of the hydrophilic polymer, but not of the crosslinked hydrophilic polymer.

For these reasons alone, the combination of Rupprecht, Becher and Zerbe does not teach the appellants' dosage form comprising at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydroxypropylmethylcellulose which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers and whereby the hydroxypropylmethylcellulose has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

3. The facts of *In re Aller* are not analogous to the present application

MPEP 2144.04 states that "...if the facts in a prior legal decision are sufficiently similar to those in an application under examination, the examiner may use the rationale used by the court."

The final rejection relies notes the holding of *In re Aller* whereby when the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation, presumably to account for the fact that the combination of Rupprecht, Becher and Zerbe did not teach the "30% to 60% by weight of glycerol" limitation. The *Aller* decision is also cited in MPEP 2144.05, section II.A.

However, the very next section in the MPEP, i.e. MPEP 2144.05, section II.B, states that "[a] particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)."

When facts of the presently claimed invention and prior art relied upon are considered, there is no inference from any of Rupprecht, Becher or Zerbe that optimizing the amount of

glycerol would have constituted a results effect variable within the context of their respective inventions and certainly does not suggest a correlation between the amount of glycerol and cross-linked hydroxypropylmethylcellulose as is claimed by the appellants.

Furthermore, as noted in the appellants' description of the state of the art, the amount of plasticizer was not thought of as being a results effective variable, i.e. amounts of plasticizer over 20% by weight were thought to produce deleterious effects. It was surprising that the selection of a specific type of crosslinked hydrophilic polymers (hydroxypropylmethylcellulose) and specific type of plasticizer (glycerol) would allow for greater content of glycerol than thought possible by those of skill in the art prior to the appellant's claimed invention.

4. Appellants disclosed evidence of unexpected results

As noted in the appellants' description of the state of the art, other types of plasticizers, e.g. triethyl citrate, did not result in the desired effects for a dosage form.

The appellants also tested against other plasticizers, including those cited in Becher and Zerbe (i.e. polyethylene glycol) and showed evidence of unexpected results.

Figures 1 and 3 in the appellants' specification showed that the use of glycerol in amounts greater than 20% by weight resulted in more desirable products that when polyethylene glycol, sorbitol or triethylcitrate were used as plasticizers and that even when comparing glycerol against itself (20% by weight vs. 50% by weight) a more favorable product was obtained at the higher levels of glycerol content (see Figure 2).

C. 35 U.S.C. 103(a) rejection (Claims 1, 6-15 and 18-22 - Rupprecht, Becher, Lydzinski)

The combination of Rupprecht, Becher and Lydzinski is essentially a duplicate rejection of Rupprecht, Becher and Zerbe wherein Lydzinski constitutes a weaker reference than Zerbe. As such, the appellants' arguments presented above against the combination of Rupprecht, Becher and Zerbe are also applicable here and are incorporated by reference.

For the sake of completeness, the appellants note that Lydzinski refers to an oral film containing chemically modified ***starch*** (chemical modification can include crosslinking, but starch is not hydroxypropylmethylcellulose). Potential plasticizers, among others include polyols such as glycerol, but also propylene glycol and sorbitol. Other potential plasticizers include polyesters such as triethyl citrate. (see paragraph [0026] of Lydzinski)

It is not surprising that paragraph [0026] of Lydzinski states that "the plasticizer may be present in any desired amount, particularly from 0 to about 15 percent, more particularly from 0 to about 10 [percent] by weight of the starch component" as these lower ranges are consistent with the state of the art described by the appellants in their specification and repeated in the "Background" section of B.1. above.

Therefore, Lydzinski does not aid in asserting that the combination of Rupprecht, Becher and Lydzinski teaches the appellants' dosage form comprising at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydroxypropylmethylcellulose which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers and whereby the hydroxypropylmethylcellulose has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

(VIII) CLAIMS APPENDIX

1. (Previously presented)

A dosage form in film form for transmucosal or transdermal administration of at least one active ingredient and/or nutrient to a living creature comprising

at least one active ingredient-containing and/or nutrient-containing layer based on in-situ crosslinked hydrophilic polymers which comprises from 30% to 60% by weight of glycerol as plasticizer, based on the total amount of crosslinked hydrophilic polymers

characterized in that hydroxypropylmethylcellulose is used as hydrophilic polymer and the hydrophilic polymer has been crosslinked with tannin and/or a crosslinked, optionally partially neutralized polyacrylic acid.

2-5. (Cancelled)

6. (Previously presented)

The dosage form as claimed in claim 1, characterized in that the active ingredient-containing and/or nutrient-containing layer comprises at least one active pharmaceutical ingredient or one nutrient.

7. (Original)

The dosage form as claimed in claim 6, characterized in that the active pharmaceutical ingredient is an active ingredient from the group of analgesics, antiallergics, antibiotics, antiemetics, antiseptics, antihistamines, antihypertensives, appetite suppressants, cardiac remedies, chemotherapeutic agents, enzymes, hormones, immunomodulators, inoculations, local anesthetics, psychoactive drugs, spasmolytics, virustatics, vitamins and cytostatics.

8. (Original)

The dosage form as claimed in claim 6, characterized in that the nutrient is a fertilizer.

9. (Previously presented)

The dosage form as claimed in claim 1, characterized in that it has one or more layers.

10. (Original)

The dosage form as claimed in claim 9, characterized in that it has at least one active ingredient-containing and/or nutrient-containing layer, one adhesive layer and/or one covering layer.

11. (Original)

The dosage form as claimed in claim 10, characterized in that at least one active ingredient-containing and/or nutrient-containing layer has a concentration gradient of the active ingredient and/or of the nutrient.

12. (Original)

The dosage form as claimed in claim 10, characterized in that the covering layer is impermeable for the active ingredient.

13. (Previously presented)

The dosage form as claimed in claim 1, characterized in that it is covered by a protective layer before application.

14. (Previously presented)

The dosage form as claimed in claim 1, characterized in that the living creature is a human or an animal.

15. (Previously presented)

The dosage form as claimed in claim 1, characterized in that the transmucosal or transdermal administration is buccal administration.

16-17 (Cancelled)

18. (Previously presented)

The dosage form as claimed in claim 1, characterized in that it has at least one active ingredient-containing and/or nutrient-containing layer, one adhesive layer and/or one covering layer.

19. (Previously presented)

The dosage form as claimed in claim 18, characterized in that at least one active ingredient-containing and/or nutrient-containing layer has a concentration gradient of the active ingredient and/or of the nutrient.

20. (Previously presented)

The dosage form as claimed in claim 19, characterized in that the covering layer is impermeable for the active ingredient.

21. (Previously presented)

The dosage form as claim in claim 20, characterized in that the ratio of hydrophilic polymer to crosslinker is from 2:1 to 5:1 by weight.

22. (Previously presented)

The dosage form as claimed in claim 21, characterized in that the at least one active ingredient and/or nutrient is prednisolone.

(IX) EVIDENCE APPENDIX

None

(X) RELATED PROCEEDINGS APPENDIX

None

CONCLUSION

In view of the foregoing, it is respectfully submitted that the claims on appeal are patentable and that the rejection under 35 U.S.C. §103(a) should be reversed.

Respectfully submitted,

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